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Full Report

Totally Laparoscopic Versus Open Gastrectomy for Gastric Cancer: A Matched Cohort Study

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Abstract

Background: The role of laparoscopic surgery for the treatment of gastric cancer is still controversial, particularly in terms of oncologic efficacy. The aim of this study was to compare short-term outcomes of laparoscopic and open resection for gastric cancer at a single Western institution.

Subjects and Methods: This study was designed as a matched cohort study from a prospective gastric cancer database. Forty-one patients undergoing laparoscopic gastrectomy for gastric cancer between June 2008 and January 2012 were matched with 41 patients undergoing open gastrectomy in the same time period. Patient pairing was done according to age, gender, type of gastrectomy (subtotal or total), and tumor stage via a randomized statistical method. The short-term outcomes and oncologic adequacy of the laparoscopic and open procedures were compared. A D2 lymph node dissection was performed in the majority of patients in both groups.

Results: The two study groups were similar with respect to patient and tumor characteristics. Laparoscopic procedures were associated with a decreased blood loss (118.7 versus 312.4 mL, $P < .005$), incidence of surgery-unrelated complications (3 versus 9 patients, $P < .05$), and duration of hospital stay (8.1 versus 11.5 days, $P < .05$) but increased operative time for both subtotal (223.5 versus 158.2 minutes, $P < .001$) and total (298.1 versus 185.5 minutes, $P < .001$) gastrectomies. The mean number of retrieved lymph nodes after D2 dissection was similar: 30.0 for laparoscopic and 29.7 for open patients.

Conclusions: Within the limitations of a nonrandomized analysis, this study shows that the laparoscopic approach is a safe and oncologically adequate option for the treatment of gastric cancer, which compares favorably with open gastrectomy in short-term outcomes.

Introduction

Laparoscopic surgery has been shown to provide important short-term advantages compared with open surgery for the treatment of several malignant diseases with at least the same long-term survival.[1,2] However, the role of laparoscopic surgery for the treatment of gastric cancer remains controversial. This is especially true in Western countries, where the incidence of gastric cancer and, importantly, of early lesions is much more lower than in the East.[3,4] The Western experience of laparoscopic surgery for gastric cancer is limited to the advanced forms. and only a few studies comparing laparoscopic and open gastrectomies are prospective or randomized.[5–8] However, all these studies have clearly shown that the laparoscopic approach can actually reduce surgical trauma and improve the patient's quality of life during the postoperative period compared with the open procedure.[9]

Some skepticism still remains regarding the oncological efficacy of the laparoscopic treatment of gastric cancer, in particular on the extent of lymphadenectomy.[3,10,11] It has been definitively established that surgical resection with D2 lymph node dissection is the standard of care and the only potentially curative treatment available for advanced gastric cancer.[12–14]

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The concern is to know whether laparoscopy can reproduce the same technique as performed in open surgery and then obtain the same results in terms of lymphadenectomy. Although several Eastern trials have demonstrated the oncological safety of laparoscopically assisted distal gastrectomy for early gastric cancer,[15–19] there is a need for reliable evidence to demonstrate comparative oncological results for advanced tumors, which are more prevalent in Western series.

The present study was undertaken to compare early surgical results, especially the adequacy of lymphadenectomy, between the laparoscopic and open approach for subtotal and total gastrectomy in the treatment of gastric cancer at a single Western center.

Subjects and Methods

Study design and data collection

Using a prospectively maintained gastric cancer database, all patients from June 2008 to January 2012 who underwent curative R0 surgery for gastric adenocarcinoma at the Center of Oncologic Minimally Invasive Surgery of the University of Florence, Florence, Italy, were identified. Of these patients, 41 underwent laparoscopic subtotal or total gastrectomies and were compared with 41 matched patients who underwent open subtotal or total gastrectomies in the same time period. Patient pairing was done according to age, gender, type of gastrectomy (subtotal or total), and tumor stage via a randomized statistical method. All patients underwent diagnostic and preoperative staging work-up according to a standard protocol, which includes upper digestive endoscopy with gastric biopsy and computed tomography of the abdomen and chest. Patients with distant metastases, para-aortic lymph node involvement, and/or pre- or intraoperative diagnosis of T4 lesions (i.e., local invasion of other organs, including spleen, pancreas, or peritoneum), were excluded from the study. All patients have been thoroughly informed about the study and gave written consent for the investigation in accordance with the ethical guidelines of our university.

The characteristics of patients, such as age, gender, body mass index, history of abdominal surgery, co-morbidities, and surgical outcomes (operative time, blood loss, postoperative morbidity and mortality, time-to-first flatus, time-to-first oral intake, postoperative hospitalization and pathological results) were examined.

The type of gastric resection, subtotal or total, was determined according to tumor localization, classified as upper, middle, and lower third of the stomach. The extension of lymph node dissection, namely D1 + α/β or D2, was performed according to the lymph node classification of the Japanese Gastric Cancer Association.[20] Tumors were classified according to the 7th edition of American Joint Committee on Cancer/TNM tumor staging.[21] They were also classified according to Lauren's histotype (i.e., intestinal, diffuse, or mixed).

Surgical technique

Laparoscopic subtotal gastrectomy. Under general anesthesia, the patient was placed in the supine, reverse Trendelenburg position with legs abducted. The surgeon stood between the legs of the patient. Four trocars were used. One 10–12-mm trocar for the laparoscope was inserted into the umbilicus. Another 10–12-mm trocar was inserted in the left midclavicular line 2 cm above the umbilicus as a major hand port. Two other 5-mm trocars were inserted in the right midclavicular line 2 cm above the umbilicus and in the midline just below the xiphoid process. First, a routine exploration of the abdominal cavity was performed.

The operative strategy involved 11 steps: (1) partial dissection of the left greater omentum (until the gastric short vessels) and the lymph nodes along the left gastroepiploic vessels (number 4sb); (2) dissection of the right omentum and the lymph nodes along the right gastroepiploic vessels (number 4d); (3) exposure of Henle's trunk and division of the right gastroepiploic vein and artery for dissection of infrapyloric nodes (number 6); (4) transection of the duodenum just distal to the pyloric ring and reinforcement of the stump with either interrupted stitches or a barbed running suture (V-loc; Covidien Ltd., Norwalk, CT); (5) division of the right gastric artery and dissection of the suprapyloric nodes (number 5) and the nodes along the proper hepatic artery (number 12a); (6) dissection of the nodes along the common hepatic artery (number 8) and the proximal splenic artery (number 11p); (7) division of the left gastric vein and artery and dissection of the nodes around these vessels (number 7) and the celiac trunk (number 9); (8) dissection of the lymph nodes along the lesser curvature (number 3) and the right cardiac nodes (number 1); (9) transection of the stomach on the upper third at least 5 cm above the tumor; (10) mechanical intracorporeal gastrojejunum anastomosis (either Billroth II or Roux-en-Y); and (11) mechanical extra- or intracorporeal jejunum–jejunal anastomosis. Tissue and lymph node dissection was performed using an ultrasonic scalpel (Ethicon Endo-Surgery, Cincinnati, OH). The specimen was placed in a polyethylene endobag and pulled out of the peritoneal cavity through the umbilical port, which was extended to a length of 4–6 cm.

Laparoscopic total gastrectomy. All steps of lymph node dissection were performed as for subtotal gastrectomy with the differences of a complete dissection of the left greater omentum, division of short gastric vessels (number 4a), dissection of lymph nodes along the distal splenic artery (number 11d), and dissection of left cardiac lymph nodes (number 2). The distal esophagus was transected with a linear stapler, and a Roux-en-Y intracorporeal linear side-to-side esophagojejunal anastomosis was performed in the first five procedures. In the last 7 patients, we used the newly developed transorally inserted anvil (OrVil™; Covidien) and a circular stapler (EEA25; Covidien) to perform an intracorporeal circular esophagojejunostomy.[22] The specimen was pulled out through the umbilical port when a linear anastomosis was performed or through the left subcostal port extended to 4–6 cm when the OrVil device was used. The jejunum–jejunostomy was constructed with a linear stapler via these two minilaparotomies.

Open subtotal and total gastrectomy. Open gastrectomies were performed through a median incision. All steps of lymph node dissection were performed as in the laparoscopic procedures. Either Billroth II or Roux-en-Y gastrojejunum anastomoses were used after subtotal gastrectomy, whereas a Roux-en-Y circular stapling esophagojejunostomy was performed after total gastrectomy.

Statistical analysis

Matched open cases were randomly selected from the entire group of curative-intent gastrectomies performed at our institution during the same period as the laparoscopic group (LG) via a statistical randomly generated list using SPSS software package (SPSS, Inc., Chicago, IL). We performed an intention-to-treat analysis to compare short-term surgical outcomes, such as operative time, estimated blood loss, time-to-first flatus, time-to-first oral feeding, surgery-related and unrelated complications, length of stay, tumor characteristics, surgical margins, and lymph node retrieval. Categorical variables within the two study groups were compared using the chi-squared test and Fisher's exact test. Quantitative variables were summarized by either mean ± standard error of the mean values or median and range. Groups were compared using the Mann–Whitney test. All of the P values resulted from the use of two-sided statistical tests; P values < .05 were considered statistically significant.

Results

Patient characteristics

Eighty-two case-matched patients were assessed (41 LG versus 41 open group [OG]). The LG patients included 24 men (58.5%), and the median age was 73 years (range, 47–87 years). The OG patients included 25 men (61.0%), and the median age was 74 years (range, 35–90 years). No statistically significant differences were observed between the two groups according to age, gender, body mass index, number of prior abdominal operations, and co-morbidities (Table 1). None of the patients in the two groups had undergone neoadjuvant chemotherapy.

Table 1. Demographic Characteristics of Patients Undergoing Laparoscopic and Open Gastrectomy

	Laparoscopic group (n = 41)	*Open group (n = 41)*	P *value*
Gender (male/female)	24/17	25/16	NS
Age (years) [median (range)]	73 (47–87)	74 (35–90)	NS
BMI (kg/m^2) [median (range)]	26.0 (23–30)	25.0 (19–31)	NS
Previous abdominal surgery (total)	9 (21.9%)	10 (24.3%)	NS
Cholecystectomy	5 (12.2%)	3 (7.3%)	
Appendicectomy	3 (7.3%)	4 (9.7%)	
Hysterectomy	0 (0%)	1 (2.4%)	
Anterior resection of the rectum	1 (2.4%)	0 (0%)	
Ovariectomy	0 (0%)	2 (4.9%)	
Co-morbidities (total)	13 (31.7%)	12 (29.2%)	NS
Hypertension	9 (21.9%)	10 (24.3%)	
Diabetes mellitus	4 (9.7%)	3 (7.3%)	
Heart diseases	3 (7.3%)	2 (4.9%)	
Chronic lung diseases	1 (2.4%)	2 (4.9%)	
Liver cirrhosis	1 (2.4%)	0 (0%)	
Others	1 (2.4%)	1 (2.4%)	

BMI, body mass index; NS, not significant.

Operative outcomes and complications

No LG patients were converted to the open procedure. Subtotal gastrectomy was performed in 29 patients (70.7%) in both groups with Billroth II anastomosis in 19 patients and Roux-en-Y anastomosis in 10 patients in the LG compared with 16 patients with Billroth II reconstruction and 13 with Roux-en-Y anastomosis in the OG (Table 2). No statistically significant differences were found between the two groups according to these operative characteristics (Table 2). The extent of lymph node dissection was not statistically different between the two study groups, with a D2 procedure performed in most patients (37 patients [90.2%] in the LG and 39 [95.1%] in the OG) (Table 2). Mean operative time was 223.5 ± 8.7 and 298.1 ± 13.9 minutes for laparoscopic subtotal and total gastrectomy, respectively. In the OG, mean operative time was significantly lower than in the LG for both subtotal and total gastrectomy: 158.2 ± 9.1 and 185.5 ± 13.9 minutes, respectively (P < .001) (Table 2). In the OG, the amount of estimated intraoperative bleeding was more than in the LG (Table 2).

First flatus and oral feeding took place earlier in the LG compared with the OG (Table 3). Surgery-related complications occurred in 6 patients (14.6%) in the LG and in 5 patients (12.2%) in the OG (Table 3). Complications unrelated to surgery are shown in Table 3. There were no statistically significant differences in surgery-related complications between the two groups, whereas complications unrelated to surgery were more frequent in the OG than in the LG (Table 3). Re-operation was performed in 3 patients (7.3%) in the LG (due to focal pancreatitis, duodenal stump leakage, and stenosis of the jejunum–jejunostomy, respectively) and in 2 patients (4.9%) in the OG (due to duodenal stump leakage and anastomotic leakage, respectively) (P = not significant). Postoperative mortality within 30 days was 2.4% (1 patient because of septic complications after duodenal stump leakage) in the LG and 4.9% (2 patients, one because of septic

Table 2. Comparison of Operative Characteristics and Outcomes Between the Laparoscopic and Open Groups

	Laparoscopic group (n = 41)	*Open group (n = 41)*	P *value*
Gastrectomy extent (subtotal/total)	29/12	29/12	NS
Type of reconstruction[a]			NS
Billroth II	19 (65.5%)	16 (55.2%)	
Roux-en-Y	10 (34.5%)	13 (44.8%)	
Lymph node dissection			NS
D1 + α/β	4 (9.7%)	2 (4.9%)	
D2	37 (90.2%)	39 (95.1%)	
Mean operative time (minutes)			
Subtotal gastrectomy	223.5 ± 8.7	158.2 ± 9.1	< .001
Total gastrectomy	298.1 ± 13.9	185.5 ± 13.9	< .001
Blood loss (mL)	118.7 ± 10.7	312.4 ± 42.9	< .005

Data are mean ± standard error of the mean values or number (percentage) as indicated.
NS, not significant.
[a]Valid only for subtotal gastrectomy.

Table 3. Comparison of Postoperative Outcomes Between the Laparoscopic and Open Groups

	Laparoscopic group (n = 41)	*Open group (n = 41)*	P *value*
Time-to-first flatus (days)	3.0 ± 0.3	7.8 ± 1.1	< .01
Time-to-first oral feeding (days)	5.4 ± 0.5	9.4 ± 0.3	< .05
Surgery-related complications (total)	6 (14.6%)	5 (12.2%)	NS
Focal pancreatitis	2 (4.9%)	0 (0%)	
Duodenal stump leakage	2 (4.9%)	2 (4.9%)	
Anastomotic leakage	0 (0%)	2 (4.9%)	
Anastomotic bleeding	1 (2.4%)	0 (0%)	
Gastric stasis	0 (0%)	1 (2.4%)	
Anastomotic stenosis	1 (2.4%)	0 (0%)	
Surgery-unrelated complications (total)	3 (7.2%)	9 (21.9%)	< .05
Pleural effusion	1 (2.4%)	3 (7.3%)	
Pneumonia	0 (%)	2 (4.9%)	
Urinary tract infections	1 (2.4%)	2 (4.9%)	
Arrhythmia	1 (2.4%)	1 (2.4%)	
Deep venous thrombosis	0 (0%)	1 (2.4%)	
Re-operations	3 (7.3%)	2 (4.9%)	NS
Postoperative mortality	1 (2.4%)	2 (4.9%)	NS
Hospital length stay (days)	8.1 ± 0.5	11.5 ± 0.8	< .05

Data are mean ± standard deviation values or number (percentage).
NS, not significant.

complications after anastomotic leakage and the other because of cardiac failure) in the OG (P = not significant) (Table 3). Patient hospital length of stay after laparoscopic gastrectomy was 8.1 ± 0.5 days, compared with 11.5 ± 0.8 days among the open surgery patients ($P < .05$) (Table 3).

Table 4. Comparison of Pathological Outcomes Between the Laparoscopic and Open Groups

	Laparoscopic group (n = 41)	*Open group (n = 41)*	P *value*
Tumor location			NS
Upper third	11 (26.8%)	14 (34.1%)	
Middle third	12 (29.3%)	10 (24.4%)	
Lower third	18 (43.9%)	17 (41.5%)	
Tumor size (cm)	5.9 ± 0.6	6.1 ± 0.8	NS
Lauren's histotype			NS
Intestinal	14 (34.1%)	19 (46.4%)	
Diffuse	18 (43.9%)	15 (36.6%)	
Mixed	9 (22.0%)	7 (17.0%)	
Positive resection margin	0 (0%)	1 (2.4%)	NS
Stage distribution (number)			NS
Ia/Ib	5/7	4/7	
IIa/IIb	7/1	5/2	
IIIa/IIIb/IIIc	6/12/3	5/14/4	
Number of retrieved lymph nodes after D2 dissection	30.0 ± 1.5	29.7 ± 2.6	NS

Data are mean ± standard deviation values or number (percentage) as indicated.
NS, not significant.

Pathological characteristics

Pathology analyses of all patients were reviewed by one pathologist (L.M.) skilled in upper gastrointestinal tumors. There were no significant differences in tumor location, size, and histotype between the two groups (Table 4). Resection margins were negative in all LG patients, whereas they were positive in 1 patient (2.4%) in the OG (Table 4).

There were no significant differences in tumor stage distribution between the two study groups (Table 4). The overall mean numbers of lymph nodes retrieved after laparoscopic and open surgery were 29.4 ± 1.6 and 28.7 ± 2.3, respectively. If only patients with D2 dissection were considered, the mean number of harvested lymph nodes in the LG patients was 30.0 ± 1.5 compared with 29.7 ± 2.6 in the OG patients (P = not significant) (Table 4).

Discussion

Radical surgical resection of the stomach with D2 lymph node dissection is still the mainstream of the treatment of advanced gastric cancer.[23] Laparoscopic gastrectomy has been shown to improve short-term results and quality of life, compared with the open technique, and has become an acceptable alternative approach in the management of early gastric cancer, especially in Japan and Korea.[24–27] The development of laparoscopic surgery for gastric cancers in the Western world has been slower because most gastric cancers are diagnosed in an advanced stage for which laparoscopic gastrectomy is not yet considered an acceptable alternative to standard open surgery.[3,4] The skepticism regarding the oncologic efficacy of laparoscopic gastrectomy is basically due to its technical complexity and concerns the feasibility of an oncologically acceptable lymphadenectomy.

The present study confirms the feasibility and safety of the laparoscopic approach for the treatment of gastric cancer. The surgery-related complications and mortality rates in our study were comparable to those of the open approach and also acceptable if compared with previously published Western reports.[5,8,28–30] One of our major complications was duodenal stump leakage. We had 2 (4.9%) patients with this complication, with one death due to septic complications. However, our incidence of duodenal stump leakage is similar to that reported by Huscher et al.[5] (5%) and Moisan et al.[29] (6.5%) but lower than that reported by Orsenigo et al.[31] (18.3%). Nowadays, we usually reinforce the duodenal stump with a running, barbed suture after the duodenal transaction in an attempt to further reduce the incidence of this complication.

Our study also confirms the typical advantages of minimally invasive surgery with reduced blood loss, times to resume oral intake, frequency of surgery-unrelated complications, and hospital stay in comparison with the open approach.[9,18,19,32] The major operative drawback noted for the laparoscopic technique was a significantly longer operative time, in particular for total gastrectomies. However, our operative times are similar to those reported by the majority of authors who have performed laparoscopic subtotal and total gastrectomies (ranging from 144 to 348 minutes),[8,33,34] and, to our knowledge, none reported operative times similar to those of open surgery. Even Taminura et al.[35] showed an average operative time of 248 minutes after 485 laparoscopic distal gastrectomies, thus emphasizing the demanding

technical aspect of this procedure. Nevertheless, it should be noted that the longer operative time in our experience did not translate into increased perioperative complications, whereas the open surgery patients showed more early surgery-unrelated complications.

The primary end point of the present study was to ascertain the oncologic efficacy of laparoscopic gastrectomy and in particular of laparoscopic D2 lymph node dissection. The number of lymph nodes needing to be excised is considered an important factor for patients' survival following gastric cancer surgery.[23,36] Nevertheless, to date there is no consensus between Eastern (mainly Japan and Korea) and Western countries regarding to what extent lymphadenectomy should be performed and, especially, how many lymph nodes should be dissected. This controversy stems from the fact that surgery outcomes in the treatment of gastric cancer are somewhat better in Asia than in the West in regard to postoperative morbidity and mortality, number of excised lymph nodes, and long-term survival.[37] It is important that this has been definitively established for the open surgery and, more recently, has been emerging even for the laparoscopic approach. As regards lymphadenctomy, the mean number of retrieved lymph nodes reported by Asian authors after laparoscopic D2 dissection ranges from 23 to 49,[18] whereas it ranges from 15 to 35 in Western observational studies.[5,7–9,29–31] Our outcomes, with a mean number of 30.0 examined lymph nodes, are comparable with these previously reported results and, importantly, are in line with Western criteria (number of lymph nodes harvested >25) regarding adequate D2 dissection and thus surgical quality for advanced gastric cancer.[38]

In conclusion, within the limitations of a nonrandomized analysis, our study contributes to the Western experience by demonstrating both the safety and oncologic efficacy of the laparoscopic approach to the resection of gastric adenocarcinoma. We also confirm that the laparoscopic approach may provide the benefit of decreased complications and faster recovery compared with the open technique.

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Disclosure Statement

No competing financial interests exist.

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